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(FILE 'HOME' ENTERED AT 10:43:56 ON 20 APR 2004)

FILE 'STNGUIDE' ENTERED AT 10:44:15 ON 20 APR 2004

FILE 'HOME' ENTERED AT 10:44:18 ON 20 APR 2004

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     FILE 'EMBASE, BIOSIS, SCISEARCH, MEDLINE, CAPLUS, TOXCENTER, DRUGU,
     ESBIOBASE, BIOTECHNO, PASCAL, CANCERLIT' ENTERED AT 10:47:12 ON 20 APR
     2004
L2         29946 S L1 AND HUMAN
L3          3679 S L2 AND (ISOLAT? OR PURIF? OR CHARACT?)
L4           648 S L3 AND PURIF?
L5           213 DUP REM L4 (435 DUPLICATES REMOVED)
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=> d l5 ibib ab 200-213

L5 ANSWER 200 OF 213 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 113
ACCESSION NUMBER: 96349807 EMBASE
DOCUMENT NUMBER: 1996349807
TITLE: The expression of **cyclooxygenase-2** (COX-2) in amnion and decidua following spontaneous labor.
AUTHOR: Fuentes A.; Spaziani E.P.; O'Brien W.F.
CORPORATE SOURCE: Arnold Palmer Children/Women Hosp., 105 West Miller Street,Orlando, FL 32806-2036, United States
SOURCE: Prostaglandins, (1996) 52/4 (261-267).
ISSN: 0090-6980 CODEN: PRGLBA
PUBLISHER IDENT.: S 0090-6980(96)00088-3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: Prostaglandins production rises dramatically during term and preterm labor. The source of this production is thought to be the fetal membranes and maternal decidua. The enzyme responsible for the conversion of arachidonic acid to the prostaglandins and related endoperoxides is variously known as prostaglandin synthase or cyclooxygenase (COX). An inducible form of this enzyme, COX-2, has been described in several tissues. The purpose of this study was to investigate a possible role for COX-2 in labor by comparing the COX-2 content in amnion and decidua from laboring and non-laboring patients. Study Design: Fetal membranes from seven normal labor and ten elective cesarean sections at term were collected immediately following delivery. The maternal age and gravity were similar between the groups. The amnion and decidua were identified, washed in sterile saline, frozen in liquid nitrogen and stored in -70°C. COX-2 expression was determined using Western Blot analysis with a **purified** COX-2 antibody. A scanning densitometer was used to quantify the bands. Results were expressed as mean ± S.D. ng/50μg protein. Results: The concentration of COX-2 in amnion of laboring women showed a twofold increase (240.0 ± 17. 6 vs. 120. 7 ± 5.1) compared to the non-labored group ($p<0.05$). The concentration in the decidua showed no significant increase during labor (38.1 ± 7.5 vs. 26.4 ± 2.1, $p>0.05$). Conclusion: We evaluated the role of COX-2 in normal labor. Our study demonstrates that COX-2 is significantly induced in the amnion following spontaneous labor. These findings suggest that the induction of amnion COX-2 may be involved in the process of **human** labor.

L5 ANSWER 201 OF 213 MEDLINE on STN
ACCESSION NUMBER: 96185012 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8612694
TITLE: Cyclooxygenases in **human** and mouse skin and cultured **human** keratinocytes: association of COX-2 expression with **human** keratinocyte differentiation.
AUTHOR: Leong J; Hughes-Fulford M; Rakhlin N; Habib A; Maclouf J; Goldyne M E
CORPORATE SOURCE: Veterans Affairs Medical Center, San Francisco 94121, USA.
SOURCE: Experimental cell research, (1996 Apr 10) 224 (1) 79-87.
Journal code: 0373226. ISSN: 0014-4827.
(Investigators: Hughes-Fulford M, Dept Veterans' Affairs, San Francisco CA)
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences

ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960613
Last Updated on STN: 19960613
Entered Medline: 19960605

AB Epidermal expression of the two isoforms of the prostaglandin H-generating cyclooxygenase (COX-1 and COX-2) was evaluated both by immunohistochemistry performed on **human** and mouse skin biopsy sections and by Western blotting of protein extracts from cultured **human** neonatal foreskin keratinocytes. In normal **human** skin, COX-1 immunostaining is observed throughout the epidermis whereas COX-2 immunostaining increases in the more differentiated, suprabasilar keratinocytes. Basal cell carcinomas express little if any COX-1 or COX-2 immunostaining whereas both isozymes are strongly expressed in squamous cell carcinomas deriving from a more differentiated layer of the epidermis. In **human** keratinocyte cultures, raising the extracellular calcium concentration, a recognized stimulus for keratinocyte differentiation, leads to an increased expression of both COX-2 protein and mRNA; expression of COX-1 protein, however, shows no significant alteration in response to calcium. Because of a recent report that failed to show COX-2 in normal mouse epidermis, we also looked for COX-1 and COX-2 immunostaining in sections of normal and acetone-treated mouse skin. In agreement with a previous report, some COX-1, but no COX-2, immunostaining is seen in normal murine epidermis. However, following acetone treatment, there is a marked increase in COX-1 expression as well as the appearance of significant COX-2 immunostaining in the basal layer. These data suggest that in **human** epidermis as well as in **human** keratinocyte cultures, the expression of COX-2 occurs as a part of normal keratinocyte differentiation whereas in murine epidermis, its constitutive expression is absent, but inducible as previously published.

L5 ANSWER 202 OF 213 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 114

ACCESSION NUMBER: 95047880 EMBASE
DOCUMENT NUMBER: 1995047880
TITLE: Differential measurement of constitutive (COX-1) and Inducible (COX-2) cyclooxygenase expression in **human** umbilical vein endothelial cells using specific immunometric enzyme immunoassays.
AUTHOR: Creminon C.; Habib A.; Maclouf J.; Pradelles P.; Grassi J.; Frobert Y.
CORPORATE SOURCE: CEA, Serv. Pharmacologie/d'Immunologie, DRIPP,91191 Gif-sur-Yvette Cedex, France
SOURCE: Biochimica et Biophysica Acta - Lipids and Lipid Metabolism, (1995) 1254/3 (341-348).
ISSN: 0005-2760 CODEN: BBLLA6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We have produced and **characterized** monoclonal antibodies (mAbs) directed against a specific carboxyterminal sequence of **human** **cyclooxygenase-2** (residues S80-598). A rabbit polyclonal antiserum was also raised against another sequence of 10 amino acids (residues 570-581) not present in **human** constitutive cyclooxygenase-1. Affinity-**purified** polyclonal antibodies, coated on microtiter plates, were used as capture antibodies in a two-site immunometric assay, with an mAb-acetylcholinesterase conjugate used as tracer. The detection limit was 500 fmol/ml of peptide C3-COX2 (residues 570-595). The assay was specific for the **cyclooxygenase-2** (COX-2 isoform, since no immunoreactivity could be detected in platelet extracts known to be rich in cyclooxygenase-1 (COX-1). In

contrast, extracts from cultured **human** umbilical vein endothelial cells challenged with 20 nM phorbol myristate acetate (PMA) showed an increase in COX-2 immunoreactivity related both to the increase m enzyme activity and the variations observed by Western blot analysis. Under these conditions, analysis of the same cell lysates with another immunometric assay specific for COX-1 revealed insignificant variation of this enzyme. The specificity of detection was further assessed by measuring the immunoreactivity of the fractions obtained after molecular sieve chromatography of control and stimulated cell extracts, and corroborated the marked enhancement of COX-2 by comparison with COX-1. Treatment of PMA-activated cells with H-7 or actinomycin D totally abolished the COX-2 signal and had little effect on COX-1. No significant variation in COX-2 immunoreactivity was observed using the inactive isomer 4α-PMA, even at 100 nM. These assays constitute the first quantitative analysis of constitutive COX-1 and of inducible COX-2 in nucleated cells at the protein level.

L5 ANSWER 203 OF 213 EMBASE on STN DUPLICATE 115

ACCESSION NUMBER: 95273903 EMBASE
DOCUMENT NUMBER: 1995273903
TITLE: Comparison of recombinant **cyclooxygenase-2** to native isoforms: Aspirin labeling of the active site.
AUTHOR: Wennogle L.P.; Liang H.; Quintavalla J.C.; Bowen B.R.; Wasvary J.; Miller D.B.; Allentoff A.; Boyer W.; Kelly M.; Marshall P.
CORPORATE SOURCE: Research Department, CIBA Pharmaceuticals Division, 556 Morris Avenue,Summit, NJ 07901, United States
SOURCE: FEBS Letters, (1995) 371/3 (315-320).
ISSN: 0014-5793 CODEN: FEBLAL
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The search for isoform-specific enzyme inhibitors has been the focus of much recent research effort. Towards this goal, **human** recombinant **cyclooxygenase-2** (EC 1.14.99.1, prostaglandin H synthase) was expressed in insect cells and **purified** to >98% purity. Recombinant enzyme was **characterized** both by physical methods and activity measurements and shown to be fully active with kinetic properties similar to native COX-2 and COX-1. After detergent extraction, the enzyme had hydrodynamic properties indistinguishable from native bovine COX-1 and corresponded to the enzyme dimer as measured with size-exclusion chromatography. Peptide mapping via Lys-C protease identified a site of N-linked glycosylation and the aspirin covalent modification site, In the presence of heme, aspirin-specifically acetylated Ser-516. The enzyme will be suitable for biophysical studies and may lead to isoform-specific enzyme inhibitors.

L5 ANSWER 204 OF 213 SCISEARCH on STN

ACCESSION NUMBER: 95:302331 SCISEARCH
THE GENUINE ARTICLE: QU833
TITLE: T-614, A NOVEL ANTIRHEUMATIC DRUG, INHIBITS BOTH THE ACTIVITY AND INDUCTION OF **CYCLOOXYGENASE-2** (COX-2) IN CULTURED FIBROBLASTS
AUTHOR: TANAKA K (Reprint); KAWASAKI H; KURATA K; AIKAWA Y; TSUKAMOTO Y; INABA T
CORPORATE SOURCE: TOYAMA CHEM CO LTD, RES LABS, 2-4-1 SHIMOOKUI, TOYAMA 930, JAPAN (Reprint)
COUNTRY OF AUTHOR: JAPAN

SOURCE: JAPANESE JOURNAL OF PHARMACOLOGY, (APR 1995) Vol. 67, No. 4, pp. 305-314.
ISSN: 0021-5198.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 36

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To elucidate the mechanism for the selective inhibition of prostaglandin E(2) (PGE(2)) productio in inflammatory tissue by T-614 (3-formylamino-7-methylsuIfonylamino- 6-phenoxy-4H-1-benzopyran-4-one), its effects on both the activity and the induction of cyclooxygenase (COX)-2 were investigated in vitro. T-614 inhibited the activity of **purified** COX-2 enzyme (IC50: 7.7 (mu g/ml), but was inactive against both COX-1 activities of microsomal and **purified** enzymes (IC50: > 300 mu g/ml). On the other hand, when the inhibition of PGE(2) production by T-614 was examined in the cultured fibroblasts stimulated with bradykinin, T-614 at 1 mu g/ml or less inhibited PGE(2) release more effectively than that in the above cell-free system. Therefore, we examined which of the COX enzymes was expressed in bradykinin-stimulated fibroblasts by using both the reverse transcriptase polymerase chain reaction (RT-PCR) and Northern blot analyses. As a result, COX-1 mRNA was constitutively expressed in the cells, whereas COX-2 mRNA was not detected without stimulation with bradykinin, but was expressed within 30 min when stimulated. Furthermore, it was found that the addition of T-614 reduced the COX-2 mRNA levels in 30 min after stimulation. These studies suggest that at least some of inhibitory effects of T-614 on prostanoids production are mediated by the synergy of the inhibition of COX-2 activity and the inhibition of induction, and such an action of T-614 may explain the pharmacological properties of this drug.

L5 ANSWER 205 OF 213 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 94:726622 SCISEARCH
THE GENUINE ARTICLE: PQ930
TITLE: SUPPRESSION OF MONOCYTE 85-KDA PHOSPHOLIPASE A(2) BY ANTISENSE AND EFFECTS ON ENDOTOXIN-INDUCED PROSTAGLANDIN BIOSYNTHESIS
AUTHOR: ROSHAK A; SATHE G; MARSHALL L A (Reprint)
CORPORATE SOURCE: SMITHKLINE BEECHAM PHARMACEUT, DEPT INFLAMMAT & RESP PHARMACOL, UW2532, 709 SWEDELAND RD, KING OF PRUSSIA, PA, 19406 (Reprint); SMITHKLINE BEECHAM PHARMACEUT, DEPT INFLAMMAT & RESP PHARMACOL, UW2532, KING OF PRUSSIA, PA, 19406; SMITHKLINE BEECHAM PHARMACEUT, DEPT MOLEC GENET, KING OF PRUSSIA, PA, 19406
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (21 OCT 1994) Vol. 269, No. 42, pp. 25999-26005.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 43

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Studies were conducted to **characterize** a **human** monocyte model where the role of the 85-kDa phospholipase A(2) (PLA(2)) in prostanoid formation could be evaluated. The presence of an immunologically related 85-kDa PLA, and type II 14-kDa PLA(2) was demonstrated in **human** monocytes and their roles examined in lipopolysaccharide (LPS)-induced monocyte prostaglandin E(2) (PGE(2)) formation. Exposure of **human** monocytes to LPS over 18 h resulted in the up-regulation of the mitogen-inducible cyclooxygenase-a and was accompanied by production and release of prostaglandin E(2) but not leukotriene C-4. This coincided with a 2-fold increase in the 85-kDa PLA(2) protein and activity levels. In contrast, there was no effect on

the type II 14-kD-like PLA(2) activity measured in the 100,000 x g particulate fraction nor did LPS induce the release of type II 14-kDa PLA(2) into the medium. Treatment with cycloheximide over 18 h resulted in a time dependent decrease in cytosolic 85-kDa PLA(2) protein and activity (half life = 4 h), but there was no change in the particulate type II 14-kDa-like PLA(2) activity. Monocytes were therefore exposed to an 85-kDa PLA(2) initiation site directed antisense oligonucleotide which specifically decreased the cytosolic 85-kDa PLA(2) protein levels and activity in a concentration-dependent manner. This had no effect on the **cyclooxygenase-2** (protein mass or the ability to convert arachidonic acid to PGE(2)) or the particulate fraction sn-2 acylhydrolytic activity but was associated with a decrease in LPS-induced PGE(2) production. Taken together, these data support a role for the cytosolic 85-kDa PLA(2) in LPS induced monocyte PGE(2) formation.

L5 ANSWER 206 OF 213 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 94:267338 SCISEARCH
THE GENUINE ARTICLE: NK184
TITLE: ACETYLATION OF **HUMAN** PROSTAGLANDIN ENDOPEROXIDE SYNTHASE-2 (**CYCLOOXYGENASE-2**) BY ASPIRIN
AUTHOR: LECOMTE M; LANEUVILLE O; JI C; DEWITT D L; SMITH W L (Reprint)
CORPORATE SOURCE: MICHIGAN STATE UNIV, DEPT BIOCHEM, 510 BIOCHEM BLDG, E LANSING, MI, 48824 (Reprint); MICHIGAN STATE UNIV, DEPT BIOCHEM, E LANSING, MI, 48824; VANDERBILT UNIV, DEPT BIOCHEM, NASHVILLE, TN, 37232
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (06 MAY 1994) Vol. 269, No. 18, pp. 13207-13215.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 57
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Aspirin (acetylsalicylate) treatment of **human** (h) prostaglandin endoperoxide H synthase (PGHS)-1 expressed in cos-1 cells caused a time-dependent inactivation of oxygenase activity. Aspirin treatment of hPGHS-2 produced an enzyme which retained oxygenase activity but formed exclusively 15-hydroxy-5,8,11,13-eicosatetraenoic acid (15 HETE) instead of PGH(2). The 15-HETE was exclusively of the 15R configuration. The K-m values for arachidonate of native and aspirin-treated hPGHS-2 were about the same suggesting that arachidonate binds to both aspirin-treated and native hPGHS-2 in a similar manner. If, as expected, the formation of 15R-HETE proceeds through abstraction of the 13proS hydrogen from arachidonate, O-2, insertion must occur from the same side as the hydrogen abstraction; with all other lipoxy-genases and cyclooxygenases, O-2 addition is antarafacial. When microsomal hPGHS-2 was incubated with [acetyl-C-14]aspirin, the enzyme was acetylated. An S516A mutant of hPGHS-2, which retains enzyme activity, was not acetylated. This indicates that Ser-516 is the site of aspirin acetylation of PGHS-2; this residue is homologous to the ''active site'' serine of PGHS-1. An S516N mutant of hPGHS-2 was catalytically active; in contrast, an S516Q mutant lacked cyclooxygenase but retained peroxidase activity. Because in the case of PGHS-1 a smaller asparagine substitution is sufficient to eliminate cyclooxygenase activity, we conclude that the active site of PGHS-2 is slightly larger than that of PGHS-1. An S516M mutant of hPGHS-2 was obtained which resembled aspirin-acetylated hPGHS-2 in that this mutant made 15R-HETE as its major product; however, unlike the aspirin-acetylated hPGHS-2, the K-m value of the S516M mutant for arachidonate was 100 times that of native hPGHS-2.

L5 ANSWER 207 OF 213 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS

RESERVED. on STN DUPLICATE 116

ACCESSION NUMBER: 94223758 EMBASE
DOCUMENT NUMBER: 1994223758
TITLE: Expression of functional **human** chorionic gonadotropin/**human** luteinizing hormone receptor gene in **human** uterine arteries.
AUTHOR: Toth P.; Li X.; Rao C.V.; Lincoln S.R.; Sanfilippo J.S.; Spinnato II J.A.; Yussman M.A.
CORPORATE SOURCE: Department of Obstetrics/Gynecology, 438 MDR Building, Louisville Univ. School of Medicine,Louisville, KY 40292, United States
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1994) 79/1 (307-315).
ISSN: 0021-972X CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The present study investigated 1) whether extra- and intramyometrial arteries contain hCG/**human** LH receptor messenger ribonucleic acid (mRNA) and receptor protein, 2) whether hCG can bind to its vascular receptors and regulate the formation of vasoactive eicosanoids, and 3) whether hCG administration for ovulation induction can affect the vascular resistance in uterine arteries. The uterine arteries contain multiple hCG/LH receptor mRNA transcripts in endothelial and smooth muscle cells. The uterine arteries also contain an 80-kilodalton immunoreactive receptor protein in endothelial and smooth muscle cells. The extra- and intramyometrial arteries and an 80- kilodalton receptor protein bind [125I]hCG, which is inhibited by excess unlabeled hCG. The receptor mRNA, receptor protein, and ligand binding are higher in smaller intramyometrial arteries than in larger extramyometrial arteries. Incubation of uterine arteries with highly **purified** hCG resulted in a dose-dependent increase in immunoreactive cyclooxygenase-1, **cyclooxygenase-2**, prostacyclin synthase, and 6-keto-prostaglandin-F(1α) and a decrease in prostaglandin-E2, thromboxane-A2 synthase, and thromboxane-B2. There was a significant decrease in the resistance index in uterine arteries, but not in common carotid arteries, by 16 h after the administration of 10,000 IU hCG for ovulation induction in women. This decrease is positively correlated with serum hCG levels, but not with progesterone or estradiol levels. In summary, these data, demonstrating the expression of functional hCG/LH receptors in **human** uterine arteries, are novel and may have important implications for physiological uterine blood flow regulation, reproductive failure, and obstetrical hemorrhage.

L5 ANSWER 208 OF 213 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 117

ACCESSION NUMBER: 94326298 EMBASE
DOCUMENT NUMBER: 1994326298
TITLE: High-level expression of active **human** **cyclooxygenase-2** in insect cells.
AUTHOR: Cromlish W.A.; Payette P.; Culp S.A.; Ouellet M.; Percival M.D.; Kennedy B.P.
CORPORATE SOURCE: Dept. of Biochemistry Mol. Biology, Merck Frosst Center Therapeutic Res., Merck Frosst Canada Inc, PO Box 1005,Pointe Claire-Dorval, Que., H9R 4P8, CAROLINE ISLANDS
SOURCE: Archives of Biochemistry and Biophysics, (1994) 314/1 (193-199).
ISSN: 0003-9861 CODEN: ABBIA4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry

037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Active **human cyclooxygenase-2** (Cox-2) was expressed at high levels in insect cells using a recombinant baculovirus. The specific activity of Cox-2 in the microsomes of infected cells was 0.51 μmol O2/min/mg and was comparable to that obtained for partially **purified** Cox-2 from ovine placenta (0.55 μmol O2/min/mg). The Cox-2 enzyme expressed in insect cells was glycosylated to varying extents and most of the cyclooxygenase activity was in the high-speed microsomal pellet. The insect-cell-expressed enzyme also showed **characteristic** 15-hydroxyeicosatetraenoic acid production after aspirin treatment and had typical inhibition profiles with a number of known nonsteroidal antiinflammatory drugs.

L5 ANSWER 209 OF 213 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 118
ACCESSION NUMBER: 94353322 EMBASE
DOCUMENT NUMBER: 1994353322
TITLE: **Purification** and **characterization** of recombinant **human cyclooxygenase-2**.
AUTHOR: Percival M.D.; Ouellet L.M.; Vincent C.J.; Yergey J.A.; Kennedy B.P.; O'Neill G.P.
CORPORATE SOURCE: Dept. Biochemistry/Molecular Biology, Merck Frosst Centre Therapeutic Res., PO Box 1005,Pointe-Claire-Dorval, Que. H9R 4P8, Canada
SOURCE: Archives of Biochemistry and Biophysics, (1994) 315/1 (111-118).
ISSN: 0003-9861 CODEN: ABBIA4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recombinant **human cyclooxygenase-2** (hCox-2, Prostaglandin G/H synthase-2) has been **purified** from baculovirus-Sf9 and vaccina virus-Cos-7 cell expression systems. The detergent-solubilized, **purified** enzyme is heterogeneous in terms of its glycosylation. The vaccinia virus hCox-2 is a mixture of two glycoforms, whereas baculovirus hCox-2 comprises at least four species. The specific cyclooxygenase activities of both enzymes are 43 μmol O2/min/mg with arachidonic acid which is within the range of values reported for ovine Cox-1. The Km values of arachidonic acid for hCox-2 and ovine Cox-1 are 0.9 and 2.7 μM, respectively. Six other C-18 and C-20 fatty acids containing at least one 1,4-cis,cis-pentadiene moiety were also identified as substrates for hCox-2. Linoleic and γ-linolenic acid were determined by mass spectrometry as being hydroxylated primarily at the C-9 and C-13 positions, whereas linolenic acid was hydroxylated primarily at the C-12 and C-16 positions. hCox-2 binds heme such that maximal activity is observed at a stoichiometry of 1.0 heme per enzyme subunit. The apparent molecular mass of hCox-2, determined by gel filtration chromatography in the presence of 2.0% β-octylglucoside, is consistent with a dimeric structure. The results of this study indicate that the physical and catalytic properties of recombinant hCox-2 are very similar to that of the extensively studied ovine Cox-1.

L5 ANSWER 210 OF 213 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 119
ACCESSION NUMBER: 94004439 EMBASE
DOCUMENT NUMBER: 1994004439
TITLE: Novel expression of functional **human** chorionic gonadotropin/luteinizing hormone receptor gene in **human** umbilical cords.

AUTHOR: Rao C.V.; Li X.; Toth P.; Lei Z.M.; Cook V.D.
CORPORATE SOURCE: Department of Obstetrics/Gynecology, School of Medicine, University of Louisville,Louisville, KY 40292, United States
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1993) 77/6 (1706-1714).
ISSN: 0021-972X CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Human** umbilical cord contains two arteries and a vein surrounded by Wharton's jelly with amnion covering the exterior surface. The cord blood and amniotic fluid contain **human** CG (hCG). Whether hCG can directly regulate cord functions is unknown. We now report that **human** umbilical cords contain a major 4.4-kilobase and minor 2.6- and 1.8-kilobase hCG/LH receptor messenger RNA transcripts. The cords also contain a 50-kilodalton immunoreactive receptor protein which can bind hCG and LH, but not hFSH or hTSH. Rat testis used as a positive tissue control contained the same major and minor receptor transcripts and an 80-kilodalton receptor protein which can bind [125I]hCG. Rat liver used as a negative control contained neither receptor transcripts nor receptor protein. The smooth muscle and endothelial cells of umbilical arteries and vein, umbilical amnion, and cells in Wharton's jelly contain the receptor transcripts and receptor protein which can bind [125I]hCG. The receptor expression was higher in umbilical vessels closer to the baby and decreased toward placenta, becoming barely detectable once the vessels were inside the placental tissue. In vitro treatment of umbilical cords with highly **purified** hCG resulted in an increase of immunoreactive cyclooxygenase-1, **cyclooxygenase-2**, prostacyclin synthase, and 6-keto- prostaglandin F(1α), little change in thromboxane A2 synthase and a decrease of prostaglandin E2 and thromboxane B2 as compared to the controls, indicating that the cord receptors are functional. In summary, these novel findings suggest that hCG present in cord blood and amniotic fluid may directly regulate the vascular tone and quite possibly other functions of **human** umbilical cord.

L5 ANSWER 211 OF 213 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 120
ACCESSION NUMBER: 93298695 EMBASE
DOCUMENT NUMBER: 1993298695
TITLE: Novel coexpression of **human** chorionic gonadotropin (hCG)/**human** luteinizing hormone receptors and their ligand hCG in **human** fallopian tubes.
AUTHOR: Lei Z.M.; Toth P.; Rao C.V.; Pridham D.
CORPORATE SOURCE: Department of Obstetrics/Gynecology, 438 MDR Building, Louisville Univ. School of Medicine,Louisville, KY 40292, United States
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1993) 77/3 (863-872).
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FILE SEGMENT: 003 Endocrinology
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SUMMARY LANGUAGE: English

AB The **human** uterus, including its blood vessels, contains hCG/**human** LH receptors. We now demonstrate that **human** fallopian tubes also contain a 4.4- kilobase hCG/LH receptor mRNA

transcript and an 80-kilodalton immunoreactive protein that can bind [125I]hCG. Tubal mucosa contain more receptor transcripts, receptor protein, and [125I] hCG binding than the tubal smooth muscle or blood vessels. **Human** fallopian tubes also contain hCG protein and a 0.6-kilobase hCGα mRNA transcript. However, very little hCG is found in tubal cell layers other than mucosa. Ampullary segments contain more hCG/LH receptors and hCG than isthmus. Secretory phase tubes contain more than proliferative phase, postpartum, or postmenopause tubes. Incubation with highly **purified** hCG resulted in an increase in catalytically active 5- lipoxygenase, cyclooxygenase-1, and **cyclooxygenase-2** enzymes in tubal tissues. In summary, **human** fallopian tubes, which have never previously been considered a direct target of hCG/LH action, express functional hCG/LH receptor gene as well as the gene of its ligand. These novel findings suggest numerous possibilities of both physiological and pathological importance in **human** fallopian tubes.

L5 ANSWER 212 OF 213 MEDLINE on STN DUPLICATE 121
ACCESSION NUMBER: 92366465 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1380156
TITLE: **Human cyclooxygenase-2** cDNA.
AUTHOR: Hla T; Neilson K
CORPORATE SOURCE: Department of Molecular Biology, Holland Laboratory, American Red Cross, Rockville, MD 20855.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1992 Aug 15) 89 (16) 7384-8. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
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AB Cyclooxygenase (Cox), also known as prostaglandin (PG) H synthase (EC 1.14.99.1), catalyzes the rate-limiting step in the formation of inflammatory PGs. A major regulatory step in PG biosynthesis is at the level of Cox: growth factors, cytokines, and tumor promoters induce Cox activity. We have cloned the second form of the Cox gene (Cox-2) from **human** umbilical vein endothelial cells (HUVEC). The cDNA encodes a polypeptide of 604 amino acids that is 61% identical to the previously **isolated human** Cox-1 polypeptide. In vitro translation of the **human** (h)Cox-2 transcript in rabbit reticulocyte lysates resulted in the synthesis of a 70-kDa protein that is immunoprecipitated by antiserum to ovine Cox. Expression of the hCox-2 open reading frame in Cos-7 monkey kidney cells results in the elaboration of cyclooxygenase activity. hCox-2 cDNA hybridizes to a 4.5-kilobase mRNA species in HUVEC, whereas the hCox-1 cDNA hybridizes to 3- and 5.3-kilobase species. Both Cox-1 and Cox-2 mRNAs are expressed in HUVEC, vascular smooth muscle cells, monocytes, and fibroblasts. Cox-2 mRNA was preferentially induced by phorbol 12-myristate 13-acetate and lipopolysaccharide in **human** endothelial cells and monocytes. Together, these data demonstrate that the Cox enzyme is encoded by at least two genes that are expressed and differentially regulated in a variety of cell types. High-level induction of the hCox-2 transcript in mesenchymal-derived inflammatory cells suggests a role in inflammatory conditions.

L5 ANSWER 213 OF 213 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1994-46604 DRUGU B P E
TITLE: **Characterization** of the mechanism of inhibition of **human cyclooxygenase-2** by anti-inflammatory drugs.

AUTHOR: Ouellet M; Percival M D
CORPORATE SOURCE: Merck-Frosst
LOCATION: Kirkland, Quebec, Canada
SOURCE: Can.J.Physiol.Pharmacol. (72, Suppl. 1, 453, 19 1 Ref.
CODEN: CJPPA3 ISSN: 0008-4212
AVAIL. OF DOC.: Merck Frosst Centre for Therapeutic Research, Kirkland, QC H9R 4P8, Canada.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The kinetic mechanism of inhibition of the **purified** form of inducible cyclooxygenase (hCox-2) by several classical NSAIDs and a selective Cox-2 inhibitor was determined. Flurbiprofen, meclofenamate and indometacin were all time-dependent inhibitors of hCox-2. None of the 3 inhibitors had a high degree of selectivity, when compared with hCox-1. NS-398 also had time-dependent inhibition of hCox-2, but was a time-independent inhibitor of hCox-1. The difference in the mechanism of inhibition was reflected in the high degree of selectivity observed for hCox-2 over hCox-1. Results demonstrate that the mechanism of inhibition of hCox-2 by classical NSAIDs is similar to that identified for ovine Cox-1. In addition, it shows the nature of time-dependency of inhibition of hCox-1 and hCox-2 greatly determines the degree of selectivity for 1 isozyme over the other. (conference abstract).